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The use of radiobiological TCP and NTCP models to validate the dose calculation algorithm and readjust the prescribed dose

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Purpose: This study introduces an advanced method to evaluate and extent the adjustment of the prescribed dose to maintain the same clinical results, when changing the dose calculation algorithm type (a), i.e density correction method to more recently type (b) algorithm, i.e AAA.
Material and methods: 10 cases with lung cancer were studied. For each case, 3 treatment plans were generated. Plan 1 was generated using type (a) algorithm, and Plan 2 using type (b) algorithm. In plan 3 the dose was calculated with type (b) algorithm using monitor units from plan 1 as input. A global analysis based on 2D and 3D gamma (γ) was made to evaluate the under / overestimation of calculated dose. Clinical evaluation was carried out using Tumour Control Probability (TCP) and Normal Tissue Complication Probabilities (NTCP) based on Uniform Equivalent Dose model. Assuming a constant TCP, the ratio "R= TCP/NTCP" and Uncomplicated Tumor Control Probability (UTCP) were calculated to measure the clinical benefit – toxicity. Wilcoxon test was used to evaluate the significance of the differences and the correlation coefficient (r) was calculated using Spearman's rank test.
Results: The dose calculated with algorithm type (b) was significantly overestimated to organs at risks while the delivered dose in MU was underestimated, $p < 0.001$. Therefore, γ maps confirmed the dosimetric results. Moreover, there were a significant difference for NTCP for lung and heart. The ratio "R" from plan 1 and plan 2 were significantly different, indicating that to maintain the same effect benefit and toxicity the prescribed dose should be readjusted.
Conclusion: We assessed the prescribed dose using the radiobiological models. The ratio of benefit was significantly changed when moving from type (a) algorithm to type (b) algorithm. This indicate that the prescribed dose should be readjusted when type (b) algorithm will be integrated in radiation oncology. A discussion between oncologist and physicist is quite necessary in order to readjust the prescribed dose.

Key words: TCP, NTCP, EUD, gamma maps.

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62 MeV Proton beams induced DNA damage in hypoxic conditions.

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Purpose: Hypoxia represents one of the most important challenges of current radiotherapy that can potentially affect the treatment planning and outcome. For the optimization of proton therapy and its application in treating hypoxic tumors such as dose and LET painting it is important to study the DNA damage response of normal cells under hypoxic and radio resistant conditions. The present study is aimed at understanding the variations in DNA double strand breaks induction and repair along prisitine and Spread-Out-Bragg-Peak Proton beams under hypoxic.
Materials and methods: DNA DSB damage and repair response was studied in AG01522 cells irradiated at various positions along the 62 MeV therapeutic protons Bragg peak at the CATANA beam line of the Institute of Nuclear Physics (INFN) Catania, Italy. Hypoxia was mimicked by using Cobalt chloride (CoCl2) and Dimethyl Sulphoxide (DMSO) was used as a Reactive Oxygen Species (ROS) scavenger. Hypoxia induction was confirmed by immunofluorescent staining of Hypoxia inducible factor-1 alpha (HIF-1α) and DNA DSB induction was quantified using p53 Binding protein-1 (53BP1) foci.
Results: The presence of DMSO and CoCl2 reduced the 53BP1 foci by 40% as compared to foci induction under normoxic conditions (30 minutes) in the cells irradiated at the entrance position of pristine beam. Cells irradiated at the Bragg peak revealed a significant induction of residual DSB damage even in presence of DMSO and CoCl2 at 24 hrs. Cells irradiated at distal end positions of the SOBP also revealed a significant induction of the 53BP1 foci irrespective of the oxygenation conditions of the medium.
Conclusions: Our results indicate the variations in the induction and repair of DNA DSBs in presence of ROS scavenger and Hypoxia along the Bragg peak. These findings can be of potential application in the tumor treatment planning of hypoxic tumors especially near the critical organs and combining DNA repair inhibitors approach.

Key words: Hypoxia, 53BP1, SOBP

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Laser accelerated ultra high dose rate protons induced DNA damage under hypoxic conditions

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Purpose: Hypoxic tumors still pose a challenge for modern radiotherapy. Hadrontherapy has gained momentum world wide as an effective modality for tumor therapy including success in inducing cell death in cancer cells under hypoxia as reported by several investigators. Significant advances in laser technologies have led to the prospect of using laser-accelerated ions, emitted in ultrashort bursts, as a future, cost-saving alternative to conventional accelerators. An understanding of the radiobiological effects at the ultrahigh dose rate delivered by these short ions pulses on human cells under hypoxic conditions is important for the development and further advancement of this technology towards clinical applications.
Materials and methods: Laser accelerated 15-18 MeV protons generated using the Nd:glass VULCAN laser system at the Rutherford Appleton Laboratory, Oxford, UK, were delivered, by a compact magnetic transport system, to cell samples at dose rates exceeding 10^9 Gy/s. Dosimetry was validated using EBT2 gafchromic films and CR-39 tracks detector. Normal human skin fibroblasts (AG01522 cells) monolayers grown in custom made stainless steel, on 3 μm thin Mylar dishes were pre-gassed with hypoxic gas mixture (95% nitrogen and 5% Carbon-di-oxide) for 4 hours and irradiated inside portable beam-line hypoxia chambers. Hypoxia induction was confirmed using HIF-1 alpha immuostaining. DNA damage and repair kinetics was studied using 53BP1 foci formation assay up to 24 hours after irradiation under both normoxic and hypoxic conditions.
Results: Our preliminary data suggests the effectiveness of Laser accelerated protons in DNA damage induction under both normoxic and hypoxic conditions. We observed a small reduction in average foci induction at initial time points in hypoxic cells, which was not seen after 2 hrs.